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Stabilisation of vesicles and vesicular dispensing systems - by replacing water bonded to polar head gps. with membrane stabilising carbohydrate(s)

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Stabilisation of vesicles and dispensing systems based on vesicles by the addn. of hydrophilic substances, lyophilisation and storage under a protecting gas atmos. and/or at deep temps. comprises adding the active ingredient either during or after formation of small unilamellar vesicles (SUV), large unilamellar vesicles (LUV) and reverse phase evapn. vesicles (REV).

The vesicles consist of a lipid, a lipid mixt., a mixt. of lipid and surfactant, a synthetic amphiphile, a mixt. of lipid and synthetic amphiphile and/or surfactants in which the water bonded to the polar head groups is replaced by membrane stabilising carbohydrates.

The vesicles are then dried, partially dried or lyophilised and opt. stored and resuspended.

BC(1-D2, 4-B1B, 4-C2, 5-B1P, 7-A2, 12-M6, 12-M11F) D(5-H)

USE/ADVANTAGE

The vesicles and vesicular dispensing systems are more stable and hence can be stored for longer than previously. Prepn. is simple and the practical possibilities for using liposomal encapsulation are broadened. The vesicles retain their original size, fusion does not take place and the active ingredient, once enclosed, remains enclosed during and after drying and resuspension. Phase sepn. is inhibited. Vesicles up to 50 nm in dia. are stabilised.

PREFERRED COMPONENTS

The membrane-stabilising carbohydrate is a mono-, di-, tri- or oligosaccharide and/or water-sol. polysaccharide, esp. D-glucose, D-fructose, sucrose, maltose, α,α-trehalose and/or cellobiose. The molar ratio of carbohydrate to lipid is more than 1:2. The carbohydrate is biodegradable.

The active ingredient is a pesticide, agrochemical, fertiliser, dyestuff, chelate former, contrast agent for processes such as computer tomography, magnetic resonance tomography or NMR spectroscopy and for the non-pharmaceutical use of vitamins, enzymes, monoclonal antibodies, hormones genes, viruses and cell organelles.

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The vesicles and vesicular dispersing systems are stored in the absence of oxygen, under a protective gas atmosphere and/or at a low temp. esp. -20 to -196°C. The vesicles are prepd. at a lipid and active ingredient concn. derived from that suitable for use and then set to the desired concn. on resuspension using distd. water or buffer opt. after removing the carbohydrate.

EXAMPLE

50 mg Pre-dried egg phosphatidyl choline, 25 mg cholesterol, 3.5 mg dicetyl phosphate, 124 mg trehalosedihydrate and 3 mg bleomycin sulphate were dispersed in 1 ml distd water by shaking over night. The dispersion was subjected to acoustic irradiation in a Russell irradiator (Brownson B12) 4 x 4 min. alternating, under a nitrogen atmosphere in an ice bath.

The sample was centrifuged for 1 hr. at 100 000 g. Any bleomycin not enclosed was removed by gel chromatography or dialysis. The SUV in the supernatant were frozen in a dry ice/alcohol bath at -70°C and dried for 3 days in a freeze dryer. The sample was resuspended with 1 ml. distd. water. Enclosed SUV of dia. less than 50 nm were produced. No free bleomycin was detected.(5pp1401CKDwgNo0/0).

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